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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,360	09/04/2001	Teruaki Sekine	2001_1248A	1329

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EXAMINER

DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 03/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/944,360

Applicant(s)

SEKINE ET AL.

Examiner

MINH-TAM DAVIS

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 January 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 5,6,22 and 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 7-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All   b) ☐ Some \*   c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.                      6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicant's election of group I, claims 1-21, species surgical treatment in Paper No. 9 is acknowledged.

Accordingly, claims 1-4, 7-21, species surgical treatment are examined in the instant application. Claims 5-6, drawn to non-elected species are withdrawn from consideration.

#### ***Claim Rejections - 35 USC § 112, SECOND PARAGRAPH***

Claims 1-4, 7-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4, 7-21 are indefinite for the use of the language "a long period of time" in claims 1-4, 7-21, which is a relative term which renders the claim indefinite. The term "a long period of time" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

This rejection could be obviated by deleting for example "a long period of time"

#### ***Claim Rejections - 35 USC § 112, FIRST PARAGRAPH***

1. Claims 1, 3-4, 7-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for preventing recurrence of liver cancer, does not reasonably provide enablement for a method for preventing recurrence

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of "any cancer". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 3-4, 7-21 are drawn to a method for preventing recurrence of cancer for a long period of time, comprising administering activated lymphocytes while performing treatment of cancer, which is surgical operation.

Claims 1, 3-4, 7-21 encompass a method for preventing recurrence of "any cancer" for a long period of time, comprising administering activated lymphocytes while performing treatment of cancer, which is surgical operation.

The specification discloses that the rate of recurrence of liver cancer when checked in 5 years after administering activated lymphocytes within three weeks and after three and six months after performing operation of the liver cancer, is significantly lower than the control (p.12-13).

One cannot extrapolate the teaching of the specification to the scope of the claims because different cancers have different etiology and characteristics, and thus it is unpredictable that recurrence of any cancer could be prevented by the claimed method.

The specification lacks guidance on the dosage, frequency of treatment and assessment of any cancer.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

2. Claims 1, 3-4, 7-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for preventing recurrence of liver cancer for 5 years, does not reasonably provide enablement for a method for preventing recurrence of cancer for "a long period of time". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 3-4, 7-21 are drawn to a method for preventing recurrence of cancer for a long period of time, comprising administering activated lymphocytes while performing treatment of cancer, which is surgical operation.

Claims 1, 3-4, 7-21 encompass a method for preventing recurrence of cancer indefinitely, comprising administering activated lymphocytes while performing treatment of cancer, which is surgical operation.

The specification discloses that the rate of recurrence of liver cancer when checked in 5 years after administering activated lymphocytes within three weeks and after three and six months after performing operation of the liver cancer, is significantly lower than the control (p.12-13).

One cannot extrapolate the teaching of the specification to the scope of the claims because recurrence of cancer is an unpredictable event, and one cannot predict when cancer recurrence would occur.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 7-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takayama et al, Sept 02, 2000, The Lancet, 356: 802-807, or Sekine T, 1994, Human cell: Official J human cell res society (Japan): 7(3): 121-4, Chakravarty, Ashim K, 1997, Current Science (Bangalore) 73(2): 201-203.

Claims 1-4, 7-21 are drawn to a method for preventing recurrence of cancer, which is liver cancer, for a long period of time, comprising administering activated lymphocytes while performing treatment of cancer, which is surgical operation. The lymphocytes are collected from a cancer patient or the other cancer patient, and cultivated for proliferation or activating, said lymphocytes having cells of more than  $1 \times 10^9$  per millimeter. The activation is in the presence of solid phase anti-CD3 antigen and interleukin 2. The activated lymphocytes are administered at least five or more times within eight months after commencing said treatment of cancer.

Takayama et al teach administration of autologous lymphocytes cultured and activated with interleukin-2 and antibody to CD3, during the first 6 months after surgery of hepatocellular carcinoma, lower recurrence rates when checked about 6 years after surgery (abstract, page 803, first column, third and fourth paragraphs, and figure 3). Takayama et al teach that the schedule is designed to transfer sufficient cells to produce a tumor response (p.803, first column, last paragraph).

Takayama et al do not teach administering activated lymphocytes while performing treatment of cancer. Takayama et al do not teach that the lymphocytes are collected from other cancer patient, and that said lymphocytes have cells of more than  $1 \times 10^9$  per milliliter.

Sekine et al teach prevention of recurrence of hepatocellular carcinoma after curative operation, by infusion of autologous lymphocytes that have been activated and expanded by cultivation with immobilized anti-CD-3 antibody and IL-2 (abstract).

Chakravarty et al teach that reappearance of fibrosarcoma in mice is prevented after surgical removal of solid tumor, comprising administering activated syngeneic lymphocytes.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use the method of Takayama et al or Sekine et al for preventing recurrence of liver cancer after surgery. It would have been obvious to administer activated lymphocytes while performing treatment of cancer, because one would have expected that the same result would be obtained, wherein treatment with activated lymphocytes is complementary to surgery. It would have been obvious that the lymphocytes are collected from other cancer patient, to provide more lymphocytes. With regards to the amounts of lymphocytes recited in claims 12-15, to determine optimum concentration of reactants is within the level of ordinary skill in the art. See *In re Kronig*, 190 USPQ 425.

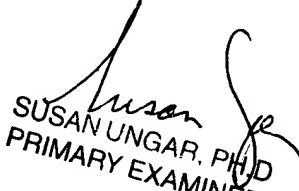
Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

March 7, 2003

  
SUSAN UNGAR, PH.D  
PRIMARY EXAMINER